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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,911	06/01/2005	Tore Duvold	3893-0200PUS2	4486

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EXAMINER	
CLARK, SARA E	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
05/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/509,911	DUVOLD, TORE	
	Examiner	Art Unit	
	SARA E. CLARK	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-10,12-15,18,19,21,24,26,27,33 and 37* is/are pending in the application.

4a) Of the above claim(s) *3,8-10,12-15,18,19,21 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6, 7, 26, 27, 33, and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/4/2004 and 1/4/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL REJECTION

This application is a 35 U.S.C. 371 (national stage) application of PCT/DK03/00220, filed 4/4/2003, which claims benefit of priority to provisional application 60/369,864, filed 4/5/2002. Claims 1-3, 6-10, 12-15, 18, 19, 21, 24, 26, 27, 33, and 37, as amended, are pending.

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-10, 12-15, 17-21, and 23-27) in the reply filed on 4/1/2009 is acknowledged. The traversal is on the ground(s) that (a) the reference cited by the examiner in the restriction requirement dated 2/23/2009 does not disclose compounds falling within the scope of the presently amended claims, and (b) there would be no undue burden to examine the full scope of all the claims. This is not found persuasive because (a) Bellini et al. does disclose compounds falling within the scope of currently amended claim 1, which can include compounds as simple as a saturated steroid nucleus with a methyl group and a carboxyl group at C20; and (b) undue burden is not a factor in unity of invention practice in 371 applications (see MPEP §§1850, 1893). However, the requirement for restriction is discretionary and has been withdrawn, such that Groups I and II have been rejoined. .

2. Applicant's species election with traverse of compound 101 in the reply filed on 4/1/2009 is acknowledged. The traversal is on the ground(s) that there would be no undue burden to examine the full scope of all the claims. This is not found persuasive because it does not address the standard under unity of invention practice in 371

applications (see MPEP §§1850, 1893). Applicant also notes that this species reads on claims 1, 2, 4, 5, 9, 10, 12, 13, 14, and 18. However, currently amended claims 4 and 5 have been canceled, and the examiner has determined that compound 101 falls within the genus (Ib) recited by claim 37, not the genus (Ia) recited by claim 10. Therefore, examiner finds that the elected compound reads on claims 1, 2, 6, 7, 26, 27, 33, and 37.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 3, 8-10, 12-15, 18, 19, 21, and 24 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/1/2009.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: the application data sheet identifies the instant application as a national stage of a provisional application, which is not the correct relationship; and incorrectly identifies the priority date as 4/5/2004.

5. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119(e), a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the

reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional

information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

6. The information disclosure statements (IDS) submitted on 10/4/2004 and 1/4/2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

7. The use of the trademark such as "FUCIDIN" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infection, does not reasonably provide enablement for preventing the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary.

When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation. Claim 33 is drawn to a method of preventing or treating a bacterial infection by administering the claimed compounds. While the medical arts teach various treatment regimens for bacterial infections, the

instant claims recite "preventing," suggesting that the disease will never develop under any conditions after administration of the composition. Applicant has not demonstrated prevention or curing of any of bacterial infection *in vitro* or in an animal model in order to provide a reasonable nexus between the compounds instantly claimed and the prevention of any bacterial infection.

While the invention may be enabled for treatment/amelioration in vitro, it is not enabled for preventing, i.e., curing, any bacterial infection *in vivo*. The unpredictability associated with treating infections, particularly those caused by antibiotic-resistant pathogens, underscores the need to provide teachings in the specification that would provide the skilled artisan with specific preventive regimens; however, the present specification does not provide such guidance and fails to provide evidence that the claimed compounds are actually capable of preventing or curing any bacterial infection. Without such guidance in the specification and the lack of correlative working examples, the claims would require an undue experimentation without a predictable degree of success on the part of the skilled artisan.

Claim Rejections - 35 USC § 112

Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In the present instance, claim 1 recites the broad recitations

- "R2 represents –COOH or $–(Z)_n$-$(NR-Z)_p$-$N(R)_2$ or $–C(O)$-$(Z)_n$-$(NR-Z)_p$-$N(R)_2$, wherein n is 0 or 1 and p is an integer from 1 and 5,"
- "R11 represents hydrogen, halogen, hydroxyl, -OSO3, -O-acyl, $–(Z)_n$-$(NR-Z)_p$-$N(R)_2$ or $–C(O)$-$(Z)_n$-$(NR-Z)_p$-$N(R)_2$,
- "provided that at least one of R2 and R11 is $–(Z)_n$-$(NR-Z)_p$-$N(R)_2$ or $–C(O)$-$(Z)_n$-$(NR-Z)_p$-$N(R)_2$."

However, claim 1 also recites "wherein R2 and/or R11 represents a moiety of the formula VIII, IX, X, XI, XII, XIII, XVI, XVII, XVIII, XIX, XX, XXI, XXII, or XXIII," which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 2, 6, 7, 26, 27, 33, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (J. Cont. Rel. 22, 223-37, 1992), in view of Mintz et al. (US Pat. 5,744,453, issued 4/28/1998).

Lee et al. disclose derivatives of 24,25-dihydrofusidic acid having a saturated steroid nucleus with the following substituents:

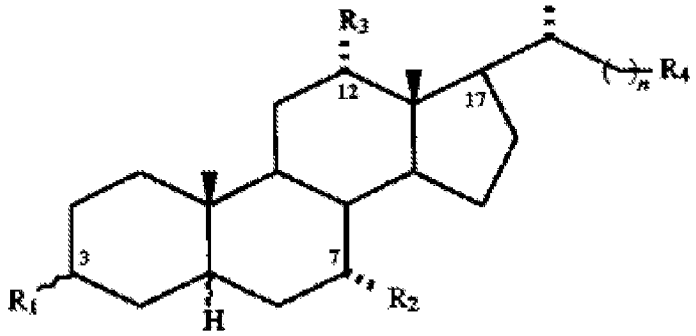
- methyl groups at C_4, C_8, C_{10}, and C_{14}, corresponding to R10, R6, R14, and R18 of formula (I) as recited in claim 1, and to the four methyl groups of formula (IB) as recited in claim 37;
- hydroxyl groups at C_3 and C_{11}, corresponding to the hydroxyl groups at R11 and R16 of formula (I) as recited in claims 1 and 7, and of formula (IB) as recited in claim 37;
- an -OAc (O-C(O)-CH_3) group at C_{16}, corresponding to the acetoxy group at R3 of formula (I) as recited in claims 1 and 6, and of formula (IB) as recited in claim 37;
- a double bond between C_{17} and C_{20}, as shown in formulae (I) and (IB) as recited in claims 1 and 37, respectively;

- a branched, unsaturated C_6 alkyl (4-methylpentyl) stemming from C_{20}, corresponding to R1 of formulae (I) and (IB) as recited in claims 1 and 37, respectively.

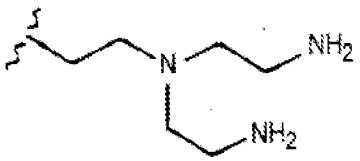
(p. 230, Table 1). Further, Lee et al. disclose straight-chain polyamine groups bonded to the carbonyl carbon C_{21} (p. 230, Table 1; see especially compounds 2, 5, and 12). However, Lee et al. do not disclose the branched polyamine side chains recited in claim 1 (specifically, that of formula VIII of elected compound 101, or those of formulae IX, X, XI, XII, XIII, XVI, XVII, XVIII, XIX, XX, XXI, XXII, or XXIII), or a single bond between C_{17} and C_{20}, corresponding to the 17,20,24,25-tetrahydrofusidic acid of elected compound 101.

Mintz et al. disclose cholic acid derivatives with a straight-chain or branched polyamine substituent at C_{21}, and methods of using such compounds as antibiotics in the treatment of bacterial infections (fig. 1; col. 1, line 37 to col. 2, line 13). Specifically, Mintz et al. teach a saturated steroid nucleus wherein

- carbon 3 can be substituted by a hydroxyl group (-OH), corresponding to R_{11} of formula (I) as recited in claims 1 and 7 and formula (IB) of claim 37;
- carbons 10 is substituted by a methyl group ($-CH_3$), corresponding to R_{14} of formula (I) as recited in claim 1 and formula (IB) of claim 37; and
- a single bond connects carbons 17 and 20, as recited in formula (I) of claim 1 and formula (IB) of claim 37.



In particular, Mintz et al. teach branched polyamine side chains starting at R_4 (C_{21}), including branched aliphatic polyamines (col. 4, lines 47-60); examples of branched polyamine substituents bonded to C_{20} are shown in figure 1 and Table 1. As disclosed in formula (I) of Mintz et al., R_4 can be defined as –C(O)-NH-R_6, in which R_6 represents an alkyl group further substituted by amino groups (col. 1, line 56 to col. 2, line 5). Thus, where R_6 is –CH_2CH_2-N(CH_2CH_2-NH_2)$_2$, as shown here,



Mintz teaches a branched polyamine side chain bonded to a carbonyl carbon C_{21}, in turn bonded to C_{20}, which is identical to claimed formula VIII as recited in claim 1, and therefore identical to the branched polyamine side chain bonded to C_{20} of elected compound 101, as recited in claim 26.

Mintz et al. also discloses formulating these branched polyamine cholic acid derivatives in pharmaceutical compositions (col. 6, lines 24-55; col. 8, lines 32-56), as recited in claim 27, as well as methods of administering these compounds and

compositions to human patients in the treatment of bacterial infections (col. 5, line 59 to col. 6, line 23), as recited in claim 33.

In summary, Lee et al. disclose derivatives of 24,25-dihydrofusidic acid having a straight-chain polyamine group bonded to the carbonyl carbon C_{21}, while Mintz et al. teach 17,20-dihydro cholic acid derivatives having the branched polyamine side chain of formula VIII bonded to the carbonyl carbon C_{21}.

One of ordinary skill in the art would have been motivated to substitute the straight-chain polyamine group bonded to the carbonyl carbon C_{21} of the 24,25-dihydro-fusidic acid derivatives as taught by Lee et al. with the branched polyamine side chain of formula VIII at the same position, with a single bond between C_{17} and C_{20}, as taught by Mintz et al., because Mintz et al. teach fusidic acid as an effective antibacterial agent that could be co-administered with their antibacterial branched polyamine cholic acid derivatives for the augmented or enhanced treatment of infection (col. 8, lines 32-56). Because both Lee et al. and Mintz et al. teach a polyamine side chain at the C_{21} carbonyl carbon of a saturated steroid nucleus, combining branched polyamines with known antimicrobial activity, as taught by Mintz et al., with a steroid moiety also with established antimicrobial activity (rather than simply a "carrier" steroid) as taught by Lee et al., would have been predicted to result in compounds having enhanced antimicrobial activity with a reasonable expectation of success. Further, as recognized by MPEP § 2144.08,

> similar properties may normally be presumed when compounds are very close in structure. *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close structural similarities and similar utilities, without more a *prima facie* case may be made.") Thus, evidence of similar properties or evidence of any

> useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. *Dillon*, 919 F.2d at 697-98, 16 USPQ2d at 1905; *In re Wilder*, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the straight-chain polyamine group at C_{21} of the 24,25-dihydro-fusidic acid derivatives as taught by Lee et al., with the branched polyamine side chain of formula VIII at the same position, with a single bond between C_{17} and C_{20}, as taught by Mintz et al., to arrive at the elected compound 101, because combining two moieties independently known to have antibacterial properties into one molecule would have been expected to result in compounds having improved efficacy against infection over that shown by each separately.

Conclusion

14. Claims 1, 2, 6, 7, 26, 27, 33, and 37 are rejected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612